```
Set      Items    Description
S1           0    (GP120(W)RT(W)NEF(W)GAG) OR
(ENV(W)RT(W)NEF(W)GAG)
S2           0    (RT(W)NEF(W)GAG(W)GP120) OR
(RT(W)NEF(W)GAG(W)ENV)
S3          30    (RT(5N)NEF(5N)GAG(5N)GP120) OR
(RT(5N)NEF(5N)GAG(5N)ENV)
S4      237532    (FUSION OR CHIMER? OR RECOMBINANT?)
(3N) PROTEIN
S5           7    S3 AND S4
S6           3    RD  (unique items)
S7         330    (NEF(5N)TAT(5N)GP120) OR
(NEF(5N)TAT(5N)ENV)
S8          17    S4 AND S7
S9           7    RD  (unique items)
S10         11    (GP120(W)NEF(W)TAT) OR
(ENV(W)NEF(W)TAT)
S11          3    S4 AND S10
S12          1    RD  (unique items)
```

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Set      Items   Description
S1           0   HIV (3N) (GP120 OR ENV OR ENVELOPE) (3N) (NEF OR GAG OR RT
             OR TAT) (3N) FUSION (5N) (LINK OR LINKED) (3N) PROMOTER
S2         124   HIV (3N) (GP120 OR ENV OR ENVELOPE) (3N) (NEF OR GAG OR RT
             OR TAT) (3N) (FUSION OR CHIMERA)
S3           3   S2 (S)PROMOTER
S4          79   RD S2  (unique items)
S5          63   S4 NOT PY>2002
S6          55   HIV (2N) (GP120 OR ENV OR ENVELOPE) (3N) (NEF OR GAG OR RT
             OR TAT) (5N) ((FUSION OR CHIMER?) (2N) PROTEIN)
S7          35   RD  (unique items)
S8          31   S7 NOT PY>2002
S9          23   (HIV OR (HUMAN(W)IMMUNODEFICIENCY(W)VIRUS)) (3N) (ENV OR E-
             NVELOPE OR GP120)(2N)RT(2N)GAG(2N)NEF
S10     845870   23 NOT PY>2002
S11         16   S9 NOT PY>2002
S12          4   RD  (unique items)
S13          0   (GP120(W)RT(W)NEF(W)GAG) OR (ENV(W)RT(W)NEF(W)GAG)
S14          0   (RT(W)NEF(W)GAG(W)GP120) OR (RT(W)NEF(W)GAG(W)ENV)
S15        175   (NEF(N)GP120) OR (NEF(N)ENV)
S16        115   S15 NOT PY>2002
S17         58   RD  (unique items)
S18          1   S17 AND ((FUSION OR CHIMER?)(2W)PROTEIN)
S19          6   S17 AND (FUSION OR CHIMER?)
S20          0   NEF-GP120 OR NEF-ENV OR GP120-NEF OR ENV-NEF
S21          0   GP120-NEF-TAT
S22          0   TAT-GP120-NEF OR TAT-ENV-NEF OR NEF-GP120-TAT OR NEF-ENV-T-
             AT
S23          4   (HIV OR (HUMAN(W)IMMUNODEFICIENCY(W)VIRUS)) (3N) (ENV OR E-
             NVELOPE OR GP120)(2N) (GP24 OR GP17)
S24          0   S23 AND (FUSION OR CHIMER?)
```

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Set     Items   Description
S1          0   HIV (3N) (GP120 OR ENV OR ENVELOPE) (3N) (NEF OR GAG OR RT
             OR TAT) (3N) FUSION (5N) (LINK OR LINKED) (3N) PROMOTER
S2        124   HIV (3N) (GP120 OR ENV OR ENVELOPE) (3N) (NEF OR GAG OR RT
             OR TAT) (3N) (FUSION OR CHIMERA)
S3          3   S2 (S)PROMOTER
S4         79   RD S2  (unique items)
S5         63   S4 NOT PY>2002
S6         55   HIV (2N) (GP120 OR ENV OR ENVELOPE) (3N) (NEF OR GAG OR RT
             OR TAT) (5N) ((FUSION OR CHIMER?) (2N) PROTEIN)
S7         35   RD  (unique items)
S8         31   S7 NOT PY>2002
? d s8/3,ab/2, 13-17, 20-29, 31
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Display 8/3,AB/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

12620104 PMID: 10683333

Expression of human immunodeficiency virus type 1 Gag protein precursor and envelope proteins from a vesicular stomatitis virus recombinant: high-level production of virus-like particles containing HIV envelope.

Haglund K; Forman J; Krausslich H G; Rose J K
Department of Pathology, Yale University School of Medicine, New Haven, Connecticut, 06510, USA.

Virology (UNITED STATES) Mar 1 2000, 268 (1) p112-21, ISSN 0042-6822--Print Journal Code: 0110674
Contract/Grant No.: RO1 AI 24345; AI; NIAID; RO1 AI40357; AI; NIAID
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Recombinant vesicular stomatitis viruses have been developed as high-level expression vectors which serve as effective vaccine vectors in animals (Roberts et al., 1998, J. Virol. 72, 4704-4711; Roberts et al., 1999, J. Virol. 73, 3723-3732). Here we show that two genes can be expressed simultaneously from a single, live-attenuated VSV recombinant. The genes used encode the Pr55(gag) protein precursor of HIV-1 (1.7-kb gene) and an HIV-1 envelope (Env) protein (2.4 kb gene). Our results show that VSV can accommodate up to a 40% increase in genome size with only a threefold reduction in virus titer. Recombinants expressing the Pr55(gag) protein precursor with or without Env protein produced abundant HIV virus-like particles (VLPs) in addition to bullet-shaped VSV particles. HIV Env protein expressed from a VSV recombinant also expressing Gag was specifically incorporated into the HIV VLPs but not into the VSV particles. In contrast, VSV G protein was found in both VSV particles and in HIV VLPs. Such VSV/HIV recombinants producing HIV VLPs with Env protein could be an effective source of HIV-like particles inducing both cellular and antibody-mediated immunity to HIV-1. Copyright 2000 Academic Press.

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Display 8/3,AB/13 (Item 13 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

10284627 PMID: 7826039

Polyvalent, recombinant HIV-1 virus-like particles: novel HIV-1 vaccine strategies.

Wagner R; Deml L; Wolf H
Institut fur medizinische Mikrobiologie, Regensburg, BRD.

Antibiotics and chemotherapy (SWITZERLAND) 1994, 46 p48-61, ISSN 0066-4758--Print Journal Code: 1305576
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

- end of record -

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Display 8/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10214740 PMID: 7958470
Expression of human immunodeficiency virus antigens in an attenuated Salmonella typhi vector vaccine.
Hone D M; Lewis G K; Beier M; Harris A; McDaniels T; Fouts T R
Department of Geographic Medicine, School of Medicine, University of Maryland, Baltimore.
Developments in biological standardization (SWITZERLAND) 1994, 82 p159-62, ISSN 0301-5149--Print Journal Code: 0427140
Contract/Grant No.: AI-25832; AI; NIAID; AI-32879; AI; NIAID; AI-33230; AI; NIAID; +
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Human immunodeficiency virus is known to enter the host at parenteral and mucosal sites and consequently an effective vaccine should stimulate immunity at both routes of entry. One approach toward stimulating HIV-specific mucosal and systemic immunity is the use of candidate live oral Salmonella typhi vector vaccine, strain CVD 908, which has been shown to stimulate mucosal and systemic immunity in volunteers. Using recombinant DNA techniques we constructed an expression cassette which comprises the lpp promoter (Plpp) and sequences encoding recombinant gp120 (rgp120). When the Plpp-rgp120 expression cassette is integrated into the chromosome of CVD 908 in the delta aroC allele, high levels of recombinant gp120 expression are observed. It is likely that effective immunity against HIV in humans will require immunization with multiple HIV antigens. Hence, a second expression cassette encoding two additional HIV antigens with vaccine potential, p24 (a HIV-1 gag gene product) and Nef (a putative regulator of HIV-1 gene expression) has been constructed. We plan to integrate the p24-Nef-encoding expression cassette into the aroD locus in the chromosome of CVD 908 delta aroC::rgp120 in a stable manner to produce a CVD 908-HIV vector vaccine that expresses multiple HIV antigens.

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Display 8/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09998700 PMID: 7510434
Assembly and extracellular release of chimeric HIV-1 Pr55gag retrovirus-like particles.
Wagner R; Deml L; Fliessbach H; Wanner G; Wolf H
Institut fur med. Mikrobiologie, LMU-Munchen, Federal Republic of Germany.
Virology (UNITED STATES) Apr 1994, 200 (1) p162-75, ISSN 0042-6822

--Print Journal Code: 0110674
Publishing Model Print; Erratum in Virology 1994 Jun;201(2) 424
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

The HIV-1 Pr55gag precursors were previously shown to assemble and bud from a variety of different cell types as noninfectious virus-like particles (VLPs) resembling immature HIV virions. The use of these VLPs as an immunogenic and autologous carrier component may allow the presentation of defined epitopes deduced from reading frames other than gag to the immune system, thereby avoiding the induction of adverse immune responses. In order to identify domains within Pr55gag that can be replaced by immunologically relevant epitopes without affecting its capacity to assemble into VLPs, we deleted three domains of a predicted high surface probability. Deletion of amino acids 211-241 within p24CA and amino acids 436-471 within the p6LI portion of Pr55gag had no effect on the assembly, ultrastructure, biophysical properties, and yields of mutant VLPs when expressed via recombinant vaccinia viruses in mammalian cells. Deletion of amino acids 99-154 overlapping the p17MA/p24CA cleavage site completely abolished the capacity of the gag polyprotein to form VLPs and led to a reduction of immature Pr55 VLPs released into the cell-culture supernatants when coexpressed with wild-type Pr55gag. In contrast, assembly and budding of chimeric VLPs could be demonstrated after replacing amino acids 211-241 and 436-471 by immunologically relevant epitopes derived from reading frames other than Pr55gag (e.g., V3 loop; CD4-binding-domain; nef-CTL epitope) or after fusion of these sequences to the carboxy terminus of Pr55gag. The importance of these data for the development of novel HIV candidate vaccines is discussed.

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Display 8/3,AB/16 (Item 16 from file: 155)

09885898 PMID: 7506555

Use of the recombinant chimera proteins, LacZ-Env and Gag-Env, for immunological studies on HIV-1 infection.

Morimoto M; Saitoh A; Ueba N; Nakata A; Shinagawa H
Osaka Prefectural Institute of Public Health, Japan.

AIDS research and human retroviruses (UNITED STATES) Oct 1993, 9 (10) p971-8, ISSN 0889-2229--Print Journal Code: 8709376
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

To use Env proteins as antigens for detection of the human immunodeficiency virus type-1 (HIV-1) antibodies, we attempted to overexpress the Env proteins in Escherichia coli. To study the epitopes in the Env proteins recognized by the sera of HIV carriers, various regions of the proviral DNA encoding the Env region were fused to the 3' end of the lacZ gene. The immunoblotting analysis of the LacZ-Env(512-611) and LacZ-Env(721-826) proteins with the 41 positive sera revealed that the former and the latter immunologically reacted with 100 and 78% of the sera, respectively. To avoid rare false-positive reactions due to the LacZ moiety of the fusion protein, we attempted to express the Env(512-611) alone or Gag-Env(512-611) under the control of bacteriophage T7 promoter. Although we could express only a low level of the Env(512-611) peptide in E. coli, we succeeded in producing large amounts of the Gag(121-406)-Env(512-611) and Gag(308-406)-Env(512-611) proteins as chimeric proteins. Both of these

chimera proteins strongly reacted with the 41 positive sera. We purified these proteins and analyzed the immunological reactivity by dot blot with the 60 positive sera and the 84 normal sera. As little as 20 ng of the dotted proteins was enough for the reaction with the positive sera, whereas as much as 320 ng of them did not show false-positive reactions with the normal sera. We obtained highly purified Gag-Env proteins with highly specific seroreactivity, which should be useful for diagnosis and prognosis.

- end of record -

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Display 8/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09537050 PMID: 1364028
Expression of HIV-2 Gag and Env antigens in E. coli.
Ulrich R; Siakkou H; Kruger D H
Acta virologica (CZECHOSLOVAKIA) Oct 1992, 36 (5) p491, ISSN 0001-723X--Print Journal Code: 0370401
Publishing Model Print
Document type: Letter
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

- end of record -

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Display 8/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08399746 PMID: 2178928
A tripartite HIV **-1** tat - env **-rev** fusion protein .
Salfeld J; Gottlinger H G; Sia R A; Park R E; Sodroski J G; Haseltine W A
Dana-Farber Cancer Institute, Department of Pathology, Harvard Medical School, Boston, MA 02115.
EMBO journal (ENGLAND) Mar 1990, 9 (3) p965-70, ISSN 0261-4189--Print Journal Code: 8208664
Contract/Grant No.: AI24845; AI; NIAID; AI28785; AI; NIAID; CA44460; CA; NCI; +
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
A 26 kd protein reactive with antiserum to the transactivator tat of the Human Immunodeficiency Virus Type 1 (HIV-1) has been detected in virus producing cells. The 26 kd protein is shown to be a tripartite fusion protein including coding sequences of the tat, envelope (env) and regulator of virion expression (rev) genes. Fusion of these coding sequences occurs by use of a previously undescribed exon within env. This 26 kd protein, designated tnv, has tat but no rev activity detectable with the assay used. The existence of other less abundant tat and rev related proteins in HIV-1 producing cells is also noted.

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? **Display 8/3,AB/21 (Item 21 from file: 155)**
DIALOG(R)File 155:MEDLINE(R)

07340684 PMID: 3495201
Comparison of recombinant human immunodeficiency virus gag precursor and gag/env fusion proteins and a synthetic env peptide as diagnostic reagents.
Shoeman R L; Young D; Pottathil R; Victor J; Conroy R R; Crowl R M; Coleman T; Heimer E; Lai C Y; Ganguly K; et al
Analytical biochemistry (UNITED STATES) Mar 1987, 161 (2) p370-9, ISSN 0003-2697--Print Journal Code: 0370535
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Diagnostic reagents for detection of human immunodeficiency virus (HIV) exposure with improved reliability may be provided by viral encoded proteins produced by recombinant DNA techniques or by synthetic peptides corresponding to appropriate viral epitopes. We have expressed at high levels in E. coli a gag gene segment corresponding to approximately 97% of the p55 gag precursor protein, as well as a novel gag/env fusion protein that contains antigenic determinants in common with gag p24, env gp41, and env gp120. The gag and gag/env proteins were purified from insoluble inclusion bodies by sequential extraction with increasing concentrations of urea. These components were tested for reactivity with antisera to HIV proteins and peptides. We have also chemically synthesized a peptide corresponding to env residues 578-608, representing a portion of env gp41. The final preparation of gag and gag/env proteins in 8 M urea reacted with sheep anti-HTLV-III p24 **gag** antibodies and acquired immune deficiency syndrome (AIDS) patient sera. The **gag / env fusion protein** also reacted with rabbit anti- **HIV env** 500-511 peptide antibody. Both recombinant proteins and the env peptide were suitable as reagents for evaluation of serum samples by enzyme-linked immunosorbent assay (ELISA). Results of ELISA assays utilizing the recombinant viral proteins and synthetic peptide were in good agreement with results obtained using disrupted virus as antigen in ELISA assays and immunoblotting.

- end of record -

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OK **Display 8/3,AB/22 (Item 1 from file: 73)**
DIALOG(R)File 73:EMBASE

11993913 EMBASE No: 2003101781
Construction of engineering yeast strain expressing gag-gp120 chimeric gene of HIV-1 and optimization of the expression condition
Jiang W.; Jin N.; Li Z.; Han W.
China
AUTHOR EMAIL: nyjin@yahoo.com
Chinese Journal of Microbiology and Immunology (CHIN. J. MICROBIOL. IMMUNOL.) (China) 30 SEP 2002, 22/5 (482-484)
CODEN: ZWMZD ISSN: 0254-5101
DOCUMENT TYPE: Journal ; Article
LANGUAGE: CHINESE SUMMARY LANGUAGE: ENGLISH; CHINESE
NUMBER OF REFERENCES: 7

Objective: To make up an engineering yeast strain expressing HIV-1 gag-gp120 chimeric gene. Methods: gag-gp120 chimeric gene was inserted into a yeast expression vector pHILS1 and the expression plasmid pHILGP was constructed. After the plasmids were linearized and electrotransformed into

the yeast strain GS115, an engineering yeast strain was screened by PCR. SDS-PAGE, ELISA analysis of expressed products, and the expression condition was optimized. Results: An engineering yeast strain was successfully established. The amount of the expressed protein was approximately 13% of the soluble protein in the supernatant. The expressed protein could reacted with **HIV** -1 positive serum, but the relative molecular mass (MSUBr) of **gag - gp120 fusion protein** was smaller than the expected value. Conclusion: The expressed protein has good antigen specificity and is exist in the supernatant of the culture which favors isolation and purification of interest protein.

- end of record -

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Display 8/3,AB/23 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013332969 BIOSIS NO.: 200100504808
New AIDS candidate vaccine: Naturally folded HIV gag - env chimerical protein **expressed in E. coli, formulated in novel potent adjuvant poloxidonium**
AUTHOR: Sidorovich I G (Reprint); Nikolaeva I A (Reprint); Chevalier A F (Reprint); Ignatjeva G A (Reprint); Alekseev T A (Reprint); Vazykhova F G (Reprint); Korobova S V (Reprint); Apryatin S A (Reprint)
AUTHOR ADDRESS: Lab. of Biotechnology and AIDS, Institute of Immunology RF Ministry of Health, Moscow, Russia**Russia
JOURNAL: Allergy (Copenhagen) 56 (Supplement 68): p141-142 2001 2001
MEDIUM: print
CONFERENCE/MEETING: XXth Congress of the European Academy of Allergology and Clinical Immunology Berlin, Germany May 09-13, 2001; 20010509
ISSN: 0105-4538
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

- end of record -

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Display 8/3,AB/24 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007561223 BIOSIS NO.: 199141073849
ROLE OF TNV A TRIPARTITE TAT - ENV **-REV** FUSION PROTEIN **IN** HIV **-1 REPLICATION**
BOOK TITLE: ISTITUTO SUPERIORE DI SANITA. VII INTERNATIONAL CONFERENCE ON AIDS: SCIENCE CHALLENGING AIDS; FLORENCE, ITALY, JUNE 16-21, 1991. 464P.(VOL. 1); 460P.(VOL. 2). ISTITUTO SUPERIORE DI SANITA: ROME, ITALY. PAPER
AUTHOR: GOTTLINGER H (Reprint); DORFMAN T; SODROSKI J; HASELTINE W
AUTHOR ADDRESS: DANA-FARBER CANCER INST, BOSTON, MASS 02115, USA**USA
p59 1991
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

- end of record -

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Display 8/3,AB/25 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007465250 BIOSIS NO.: 199140108141
DETECTION OF ALTERNATIVELY SPLICED HIV **-1 MESSENGER RNA AND CHARACTERIZATION OF A NOVEL** TAT - ENV FUSION PROTEIN
AUTHOR: FURTADO M (Reprint); GUPTA P; WOLINSKY S
AUTHOR ADDRESS: DEP MED, NORTHWESTERN UNIV, CHICAGO, ILL 60611, USA**USA
JOURNAL: AIDS Research and Human Retroviruses 7 (2): p173 1991
CONFERENCE/MEETING: SYMPOSIUM ON FRONTIERS IN HUMAN RETROVIROLOGY AND RELATED TOPICS HELD AT THE ANNUAL MEETING OF THE NATIONAL CANCER INSTITUTE LABORATORY OF TUMOR CELL BIOLOGY, BETHESDA, MARYLAND, USA, AUGUST 11-17, 1990. AIDS RES HUM RETROVIRUSES.
ISSN: 0889-2229
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

- end of record -

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Display 8/3,AB/26 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

09909233 Genuine Article#: 464BL Number of References: 47
Title: RNA splicing at human immunodeficiency virus type 1 3 ' splice site A2 is regulated by binding of hnRNP A/B proteins to an exonic splicing silencer element (ABSTRACT AVAILABLE)
Author(s): Bilodeau PS; Domsic JK; Mayeda A; Krainer AR; Stoltzfus CM (REPRINT)
Corporate Source: Univ Iowa,Dept Microbiol,Iowa City//IA/52242 (REPRINT); Univ Iowa,Dept Microbiol,Iowa City//IA/52242; Univ Iowa,Program Mol Biol,Iowa City//IA/52242; Univ Miami,Sch Med, Dept Biochem & Mol Biol,Miami//FL/33136; Cold Spring Harbor Lab,Cold Spring Harbor//NY/11724
Journal: JOURNAL OF VIROLOGY, 2001, V75, N18 (SEP), P8487-8497
ISSN: 0022-538X Publication date: 20010900
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
Language: English Document Type: ARTICLE
Abstract: The synthesis of human immunodeficiency virus type 1 (HIV-1) mRNAs is a complex process by which more than 30 different mRNA species are produced by alternative splicing of a single primary RNA transcript. HIV-1 splice sites are used with significantly different efficiencies, resulting in different levels of mRNA species in infected cells. Splicing of Tat mRNA, which is present at relatively low levels in infected cells, is repressed by the presence of exonic splicing silencers (ESS) within the two tat coding exons (ESS2 and ESS3). These ESS elements contain the consensus sequence PyUAG. Here we show that the efficiency of splicing at 3 ' splice site A2, which is used to generate Vpr mRNA, is also regulated by the presence of an ESS (ESSV), which has sequence homology to ESS2 and ESS3. Mutagenesis of the three PyUAG motifs within ESSV increases splicing at splice site A2, resulting in increased Vpr mRNA levels and reduced skipping of the noncoding exon flanked by A2 and D3. The increase in Vpr mRNA levels and the reduced skipping also occur when splice site D3 is mutated toward the consensus sequence. By in vitro splicing assays, we show that ESSV represses splicing when placed downstream of a heterologous splice site. A1, A1(B), A2, and B1 hnRNPs preferentially bind to ESSV RNA compared to ESSV mutant RNA. Each of these proteins, when added back to HeLa cell nuclear extracts depleted of ESSV-binding factors, is able to restore splicing repression. The results suggest that coordinate repression of HIV-1 RNA splicing is mediated by members of the hnRNP A/B protein family.

- end of record -

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Display 8/3,AB/27 (Item 2 from file: 34)

02773602 Genuine Article#: MC016 Number of References: 60

Title: ALTERNATIVE SPLICING OF HUMAN-IMMUNODEFICIENCY-VIRUS TYPE-1 MESSENGER-RNA MODULATES VIRAL PROTEIN EXPRESSION, REPLICATION, AND INFECTIVITY (Abstract Available)

Author(s): PURCELL DFJ; MARTIN MA
Corporate Source: NIAID,MOLEC MICROBIOL LAB/BETHESDA//MD/20892

Journal: JOURNAL OF VIROLOGY, 1993, V67, N11 (NOV), P6365-6378
ISSN: 0022-538X
Language: ENGLISH Document Type: ARTICLE

Abstract: Multiple RNA splicing sites exist within human immunodeficiency virus type 1 (HIV-1) genomic RNA, and these sites enable the synthesis of many mRNAs for each of several viral proteins. We evaluated the biological significance of the alternatively spliced mRNA species during productive HIV-1 infections of peripheral blood lymphocytes and human T-cell lines to determine the potential role of alternative RNA splicing in the regulation of HIV-1 replication and infection. First, we used a semiquantitative polymerase chain reaction of cDNAs that were radiolabeled for gel analysis to determine the relative abundance of the diverse array of alternatively spliced HIV-1 mRNAs. The predominant rev, tat, vpr, and env RNAs contained a minimum of noncoding sequence, but the predominant nef mRNAs were incompletely spliced and invariably included noncoding exons. Second, the effect of altered RNA processing was measured following mutagenesis of the major 5' splice donor and several cryptic, constitutive, and competing 3' splice acceptor motifs of HIV-1NL4-3. Mutations that ablated constitutive splice sites led to the activation of new cryptic sites; some of these preserved biological function. Mutations that ablated competing splice acceptor sites caused marked alterations in the pool of virus-derived mRNAs and, in some instances, in virus infectivity and/or the profile of virus proteins. The redundant RNA splicing signals in the HIV-1 genome and alternatively spliced mRNAs provides a mechanism for regulating the relative proportions of HIV-1 proteins and, in some cases, viral infectivity.

- end of record -

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Display 8/3,AB/28 (Item 3 from file: 34)

02599484 Genuine Article#: LP042 Number of References: 0
(NO REFS KEYED)

Title: DIFFERENTIAL IMMUNOREGULATORY ACTIVITY OF HIV ENV-GAG PROTEIN ON CORD-BLOOD VS ADULT PERIPHERAL-BLOOD LYMPHOCYTES (Abstract Available)

Author(s): TAKI HN; NAIR MPN; SCHWARTZ SA
Corporate Source: HURLEY MED CTR,DEPT PEDIAT/FLINT//MI/00000

Journal: PEDIATRIC AIDS AND HIV INFECTION-FETUS TO ADOLESCENT, 1993, V4, N3 (JUN), P138-143
ISSN: 1045-5418
Language: ENGLISH Document Type: ARTICLE

Abstract: We and others have shown that several peptides from HIV (e.g., TAT protein and env peptides) can modulate the activities of lymphocytes from adult donors. In this study the recombinant **HIV fusion protein env - gag** was examined for its immunoregulatory

activities on both adult peripheral blood lymphocytes (PBL) and cord blood lymphocytes (CBLs). Proliferative response of lymphocytes was determined by H-3 thymidine incorporation. While 95% of PBL samples responded with significant proliferation to the HIV peptide, only 25% of the CBL samples responded. In the same experiment, while none of PBL samples showed suppression of proliferation with the **HIV env - gag fusion protein** , 45% of the CBL samples did show suppression.

When lymphocytes were incubated simultaneously with env-gag protein and phytohemagglutinin (PHA), 75% of the CBL samples showed significant decreases in their mitogen proliferative responses, while only 8% of adult lymphocytes samples showed similar decreases. These observations suggest that HIV env-gag protein has immunoregulatory effects on lymphocytes and that this effect differs significantly in CBLs versus PBLs.

- end of record -

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Display 8/3,AB/29 (Item 4 from file: 34)

01942899 Genuine Article#: JN267 Number of References: 32

Title: PHENOTYPE-ASSOCIATED ENV GENE VARIATION AMONG 8 RELATED HUMAN-IMMUNODEFICIENCY-VIRUS TYPE-1 CLONES - EVIDENCE FOR INVIVO RECOMBINATION AND DETERMINANTS OF CYTOTROPISM OUTSIDE THE V3-DOMAIN (Abstract Available)

Author(s): GROENINK M; ANDEWEG AC; FOUCHIER RAM; BROERSEN S; VANDERJAGT RCM ; SCHUITEMAKER H; DEGOEDE REY; BOSCH ML; HUISMAN HG; TERSMETTE M
Corporate Source: UNIV AMSTERDAM,NETHERLANDS RED CROSS,BLOOD TRANSFUS SERV,CENT LAB/AMSTERDAM//NETHERLANDS/; UNIV AMSTERDAM,EXPTL & CLIN IMMUNOL LAB/AMSTERDAM//NETHERLANDS/; NATL INST PUBL HLTH & ENVIRONM PROTECT,IMMUNOBIOL LAB/BILTHOVEN//NETHERLANDS/

Journal: JOURNAL OF VIROLOGY, 1992, V66, N10 (OCT), P6175-6180
ISSN: 0022-538X
Language: ENGLISH Document Type: NOTE

Abstract: The nucleotide sequences of the env genes of eight phenotypically heterogeneous human immunodeficiency virus type 1 (HIV-1) clones recovered from a single individual within a 3-week period were compared. In addition, the accessory gene sequences for four of these clones were obtained. Variation among most accessory genes was limited. In contrast, pronounced phenotype-associated sequence variation was observed in the env gene. At least three of these clones most likely resulted from genetic recombination events in vivo, indicating that this phenomenon may account for the emergence of proviruses with novel phenotypic properties. Within the env genes of the eight clones, four domains could be defined, the sequence of each of which clustered in two groups with high internal homology but 11 to 30% cluster variation. The extensive env gene variation among these eight clones could largely be explained by the unique manner in which the alleles of these four domains were combined in each clone. Experiments with chimeric proviruses demonstrated that the HIV-1 env gene determined the capacity to induce syncytia and tropism for T-cell lines. Amino acids previously shown to be involved in gp120-CD4 and gp120-gp41 interaction were completely conserved among these eight clones. The finding of identical V3 sequences in clones differing in tropism for primary monocytes and T-cell lines demonstrated the existence of determinants of tropism outside the env V3 region.

- end of record -

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Display 8/3,AB/31 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

00806622 Genuine Article#: EY300 Number of References: 0
Title: DETECTION OF ALTERNATIVELY SPLICED HIV **-1 MESSENGER-RNAS AND CHARACTERIZATION OF A NOVEL** TAT - ENV FUSION PROTEIN
Author(s): FURTADO M; GUPTA P; WOLINSKY S
Corporate Source: UNIV PITTSBURGH,GRAD SCH PUBL HLTH/PITTSBURGH//PA/15261; NORTHWESTERN UNIV,DEPT MED/CHICAGO//IL/60611
Journal: AIDS RESEARCH AND HUMAN RETROVIRUSES, 1991, V7, N2, P173
Language: ENGLISH Document Type: MEETING ABSTRACT

08974871 PMID: 1926777
Analysis of alternatively spliced human immunodeficiency virus type-1 mRNA species, one of which encodes a novel tat-env fusion protein.
Furtado M R; Balachandran R; Gupta P; Wolinsky S M
Department of Medicine, Northwestern University Medical School, Chicago, Illinois 60611.
Virology (UNITED STATES) Nov 1991, 185 (1) p258-70, ISSN 0042-6822 --Print Journal Code: 0110674
Contract/Grant No.: AI-32535; AI; NIAID; AI-72631; AI; NIAID
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
A polymerase chain reaction-based analysis was used to define the structures of the mRNAs that encode human immunodeficiency virus type-1 (HIV-1) regulatory and structural proteins in infected H9 cells. Twenty alternatively spliced mRNAs encoding the vif, vpr, env , nef , tat, and rev proteins were characterized. An evaluation of the coding potentials of these transcripts recognized both leaky scanning and reinitiation at downstream initiation codons as mechanisms that may operate during translation of many of the polycistronic messages. Two new splice acceptor sites, one at nt 6018 defining a new mRNA coding for the env and vpu proteins and another at nt 8671 defining a novel tat-env fusion transcript, were characterized. The latter transcript expressed a novel protein p17tev that was immunoprecipitated by both polyclonal tat antibodies and monoclonals directed towards the C-terminal region of gp41. The p17tev protein was able to transactivate transcription from the HIV-1 LTR in transient transfection assays. The use of multiple alternative splice donor and acceptor sites and the generation of novel proteins may confer evolutionary advantages on the viral mutants encoding them and influence the course of clinical disease.

Set	Items	Description
S1	712	(HIV (5N) TAT) (2N) (NEF OR GAG OR RT OR GP120 OR ENV)
S2	471896	FUSION
S3	1336401	(FUSION OR CHIMER? OR RECOMBINANT)
S4	241	S1 AND S3
S5	180	S4 NOT PY>2002
S6	82	RD (unique items)
S7	75	(HIV (5N) TAT) (2N) (NEF OR GAG OR RT OR GP120 OR ENV) (3N) (FUSION OR CHIMER? OR RECOMBINANT)
S8	28	RD (unique items)
S9	19	S8 NOT PY>2002

Display 6/9/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13868324 PMID: 12163269

A novel chimeric **Rev, Tat, and Nef (Retanef) antigen as a component of an SIV/HIV vaccine.**

Hel Zdenek; Johnson Julie M; Tryniszewska Elzbieta; Tsai Wen-Po; Harrod Robert; Fullen Jake; Tartaglia Jim; Franchini Genoveffa

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Subfile: INDEX MEDICUS; Toxbib

The human immunodeficiency virus type 1 (**HIV** -1) regulatory proteins Rev, **Tat** , and **Nef** are expressed at early time post-infection and represent attractive targets to be included in a vaccine candidate for AIDS. However, the putative immunosuppressive activities of some of these proteins may limit their immunogenicity. To circumvent these issues, a novel **chimeric** polyprotein vaccine candidate (Retanef), comprising genetically modified and re-assorted rev, tat, and nef open reading frames of simian immunodeficiency virus (SIV), was constructed and optimized for its expression in mammalian cells. Retanef encodes a protein of approximately 55 kDa localized primarily in the cytoplasm of transfected cells. The Retanef gene expressed in context of an eucaryotic expression vector (DNA-SIV-Retanef) or cloned into a highly attenuated poxvirus-based NYVAC vector (NYVAC-SIV-Retanef) was used to immunize either naive rhesus macaques or macaques chronically infected with SIVmac251 undergoing anti-retroviral therapy (ART). Three immunizations of naive macaques with DNA-SIV-Retanef followed by a single NYVAC-SIV-Retanef boost induced a response to the Mamu-A(*)01-restricted Tat epitope (Tat SL8, TTPESANL) demonstrated by staining with a specific tetramer and by direct cytolytic activity assays, as well as responses to Rev, Tat and Nef proteins demonstrated by ELISPOT assays using overlapping peptide pools encompassing the entire proteins. Immunization of infected macaques with either DNA-SIV-Retanef or NYVAC-SIV-Retanef expanded the frequency of Tat-specific tetramer-staining cells by two- to seven-fold. No adverse effects were observed in either naive or SIV-infected rhesus macaques. Thus, an analogous HIV-1-based **chimeric** vaccine may represent useful component of an HIV-1 vaccine. Copyright 2002 Elsevier Science Ltd.

Descriptors: *AIDS Vaccines--genetics--GE; *Genes, nef; *Genes, rev; *Genes, tat; *HIV-1--immunology--IM; *Immunotoxins--genetics--GE; *SAIDS Vaccines--genetics--GE; *Simian immunodeficiency virus--immunology--IM; AIDS Vaccines--adverse effects--AE; AIDS Vaccines--biosynthesis--BI; AIDS Vaccines--immunology--IM; Amino Acid Sequence; Animals; Antigens, Viral --genetics--GE; Antigens, Viral--immunology--IM; Base Sequence;

Cercopithecus aethiops; Genes, env; Genetic Vectors--genetics--GE; HIV Antigens--genetics--GE; HIV Antigens--immunology--IM; HIV-1--genetics--GE; Hela Cells; Humans; Immunotoxins--immunology--IM; Macaca mulatta; Molecular Sequence Data; Open Reading Frames; Proteins; **Recombinant Fusion** Proteins--genetics--GE; **Recombinant Fusion** Proteins--immunology--IM; SAIDS Vaccines--adverse effects--AE; SAIDS Vaccines--immunology--IM; Simian immunodeficiency virus--genetics--GE; Transfection; Vaccination; Vaccines, Synthetic--adverse effects--AE; Vaccines, Synthetic--genetics --GE; Vaccines, Synthetic--immunology--IM; Vero Cells